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(54) Title: METHODS OF IDENTIFYING AGENTS EFFECTIVE TO TREAT COGNITIVE DECLINE AND DISEASES ASSOCIATED THEREWITH

(57) Abstract: Embodiments described herein are directed to methods of identifying agents effective to treat cognitive decline and diseases associated therewith. Embodiments described herein are also directed to kits for performing methods described herein. Embodiments described are also directed to methods of diagnosis and uses of the same.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 11/26530

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - G01N 33/48 (2011.01)
USPC - 435/29
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
USPC -- 435/29

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WEST -- PGPB,USPT,USOC,EPAB,JPAB; Dialog Classic Files -- 654, 652, 349, 35, 65, 155; PCT Patentscope; USPTO Web Page; Entrez Pubmed; Google Scholar; Search terms -- screen/identify agents amyloid precurors, amyloid beta, monomer, oligomer, hippocampal cell, binding assay, membrane trafficking, MTT-tetrazolium assay, kit, diagnosis, treatment, Alzh

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	US 2010/0028333 A1 (GETTY et al.) 04 February 2010 (para [0003], [0005], [0009], [0011], [0013]-[0016], [0034], [0036], [0038], [0042], [0045]-[0049], [0052]-[0054], [0057], [0058], [0062], [0063], [0068], [0073], Fig 6, 7	1-9, 13-15, 17, 18, 21, 23-34, 36-39, 42-44, 46-52, 54-58 --- 10-12, 16, 19, 20, 22, 35, 40, 41, 45, 53, 59-62
Y	TONG, L. et al. Beta-Amyloid Peptide at Sublethal Concentrations Downregulates Brain-Derived Neurotrophic Factor Functions in Cultured Cortical Neurons. Journal of Neuroscience, 28 July 2004, Vol. 24, No. 30, pages 6799-6809; pg 6799, abstract, col 1, para 1; pg 6801, col 1, para 6, col 2, para 3, Fig 1	10, 11
Y	WO 2009/059214 A1 (JIN et al.) 07 May 2009 (07.05.2009) para [0017], [0104]-[0107], [0111], [0113], [0116], [0126], Fig 7A-B	12, 16, 20, 45
Y	US 2008/0101757 A1 (EATON et al.) 17 July 2008 (17.07.2008) para [0149]	19, 35, 53
Y	US 2009/0022667 A1 (PETERS et al.) 22 January 2009 (22.01.2009) para [0027], [0057], [0116], [0117], abstract	22
Y	US 2009/0035295 A1 (HILLEN et al.) 05 February 2009 (05.02.2009) para [0004], [0101], [0102], [0117]	40, 41
Y	US 2008/0103107 A1 (WARD et al.) 01 May 2008 (01.05.2008) para [0018], [0026], [0052], [0094]	59-62

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 June 2011 (13.06.2011)	30 JUN 2011
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 11/26530

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I: Claims 1-53, directed to methods and kits for identifying agents effective to treat Alzheimer's disease, the method comprising contacting neurons with yellow tetrazonium salt and test agentst. Notably Group I does not require contacting neurons with test binding partners.

SEE CONTINUATION SHEET.

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 11/26530

Continuation of Box III

Group II: Claims 54-62, directed to methods for identifying agents effective to treat Alzheimer's disease, the method comprising contacting neurons with test binding partners. Notably Group II does not require contacting neurons with yellow tetrazolium salt or test agents.

While Groups I and II share certain technical features, these do not represent a contribution over the prior art. See, for example, US 2010/0028333 A1 to Getty et al. which teaches methods of identifying test agents (para [0011], [0013]) which affect neuron cell membrane trafficking (para [0021], [0033]), and would therefore be effective to treat Alzheimer's disease. Getty teaches contacting neurons with test agents (para [0045]).

Because these features were known at the time of the invention, they can not be considered to be special technical features that would otherwise unify these groups. Therefore, there is no unity of invention.